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Prediction of Cerebral Hyperperfusion after Carotid Endarterectomy with Transcranial Doppler

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WHAT THIS PAPER ADDS

- Cerebral hyperperfusion syndrome (CHS) after carotid endarterectomy (CEA) is potentially life threatening and therefore identification of patients at risk is essential. Intra-operative transcranial Doppler (TCD) monitoring is associated with both false positive and false negative results. In the present study we assessed the predictive values of an additional TCD measurement in the early postoperative phase. We found that postoperative TCD significantly increased both the positive and negative predictive values. Our adjusted monitoring strategy using perioperative TCD may contribute to the further reduction of adverse events after carotid revascularisation.

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ABSTRACT

Objectives: To determine the diagnostic value for predicting cerebral hyperperfusion syndrome (CHS) by adding a transcranial Doppler (TCD) measurement in the early postoperative phase after carotid endarterectomy (CEA).
Design: Patients who underwent carotid endarterectomy between January 2004 and August 2010 and in whom both intra- and postoperative TCD monitoring were performed were included.
Methods: In 184 CEA patients the mean velocity (V_{mean}) preoperatively (V_1), pre-clamping (V_2), post-declamping (V_3) and postoperatively (V_4) was measured using TCD. The intra-operative V_{mean} increase $((V_3 - V_2)/V_2)$ was compared to the postoperative increase $((V_4 - V_1)/V_1)$ in relation to CHS. CHS was diagnosed if the patient developed neurological complaints in the presence of a preoperative V_{mean} increase >100%.
Results: Sixteen patients (9%) had an intra-operative V_{mean} increase >100% and 22 patients (12%) a postoperative V_{mean} increase of >100%. In 10 patients (5%) CHS was diagnosed; two of those had an intra-operative V_{mean} increase of >100% and nine postoperative V_{mean} increase >100%. This results in a positive predictive value of 13% for the intra-operative and 41% for the postoperative measurement.
Conclusions: Besides the commonly used intra-operative TCD monitoring additional TCD measurement in the early postoperative phase is useful to more accurately predict CHS after CEA.

Carotid endarterectomy (CEA) is the standard treatment for patients with high-grade symptomatic stenosis of the internal carotid artery (ICA). Operative treatment has also been demonstrated to be superior to medical treatment in patients younger than 75 years with an asymptomatic high-grade stenosis of the ICA.

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Unfortunately, the benefits of this procedure are hampered by serious procedure-related complications resulting in perioperative death or stroke in up to 5% of patients.[1,2]

Perioperative strokes can be categorised by time of onset. Ischaemic strokes that occur during the operation and become apparent upon recovery from anaesthesia are thought to be caused by hypoperfusion during clamping or by thrombo-embolism.[3] Postoperative strokes develop after a symptom-free interval and are mainly caused by local thrombosis, thrombo-embolism or cerebral hyperperfusion syndrome (CHS).[3] Introduction of intra-operative cerebral monitoring using computerised electroencephalography (EEG) and transcranial Doppler (TCD) has significantly decreased the intra-operative stroke rate.[4–6] However, complications in the postoperative phase cannot be prevented by this approach.[7]

CHS can occur during the first few days up to 4 weeks after CEA in 1–3% of patients.[8] It is hypothesised that in a previously hypoperfused area with a disturbed autoregulation a sudden increase of blood flow may lead to cerebral hyperperfusion.[9] CHS can cause a spectrum of symptoms including headache, vomiting, neurological deficit or seizures.[10] Patients may have only mild and transient symptoms, but if not recognised and treated adequately in time (i.e., strict blood pressure control), haemorrhagic stroke and subsequent death may occur in up to 40% of patients.[11]

The generally accepted definition of postoperative cerebral hyperperfusion in the context of CEA is defined as an increase in cerebral blood flow (CBF) of >100% over baseline.[12] This occurs in approximately 10% of CEA patients[13] and has been associated with a 10-fold higher risk for postoperative intra-cerebral haemorrhage in patients operated under general anaesthesia.[12,14] Changes in CBF are correlated with changes in the mean blood velocity (V_{mean}) in the ipsilateral middle cerebral artery (MCA) as measured with TCD.[15,16] Currently, during CEA under general anaesthesia, an increase in V_{mean} of >100% 3 min after declamping the ICA, compared to the pre-clamping V_{mean} is the most commonly used predictor of CHS.[11,17–19] However, intra-operative TCD monitoring is associated with both false negative and false positive results.[11,20] Therefore, a more precise method is needed to predict which patients are at risk for CHS.

This study aimed to assess the predictive power of intra-operative TCD monitoring regarding the development of CHS, by introducing an additional TCD measurement in the first two post-operative hours.

Materials and Methods

Patients

Data were derived from two Dutch Vascular referral centres. Patients operated between February 2009 and August 2010 in the University Medical Center Utrecht (UMCU) were prospectively and patients who underwent CEA between January 2004 and August 2010 in St. Antonius Hospital, Nieuwegein, were retrospectively included. All patients who underwent CEA for a high degree ICA stenosis and in whom both intra- and postoperative TCD monitoring were performed were included.

Carotid endarterectomy

In both centres, surgery was performed under general anaesthesia and all patients received the same anaesthetic regimen. Anaesthesia was induced with propofol, sufentanil and rocuronium, and maintained with isoflurane. After tracheal intubation, mechanical ventilation was adjusted to maintain normocapnia. CEA was performed by an experienced vascular surgeon or by a vascular trainee under supervision in a standardised way. An intra-luminal shunt was used selectively in case of EEG asymmetry or a decrease of >60% of V_{mean} measured by TCD.[21] Postoperatively, patients stayed for at least 6 h on the recovery ward for continuous blood pressure (BP) monitoring.

Definition of study end points

CHS (primary end point) was diagnosed if the patient developed headache, confusion, seizures, intracranial haemorrhage or focal neurological deficits in the presence of postoperative cerebral hyperperfusion (defined as >100% increase of the preoperative V_{mean}) after a symptom-free interval. The diagnosis of CHS was made by an independent neurologist.[8]

Postoperative hypertension (PH) (secondary end point) was defined either as an absolute high BP threshold (BP >160 mmHg systolic) or as a relative high BP (20% above the preoperative BP).[22] Moreover, PH was also scored if, in patients identified as being at risk for CHS based on the intra-operative V_{mean} increase, BP was raised above the adjusted restriction (see below).[22]

Measurements

The preoperative BP was measured (non-invasively) during the preoperative TCD measurement. If these data were not available, the BP obtained during preoperative assessment was used.

In the perioperative period, BP was measured using an intra-arterial catheter in the radial or brachial artery. Systolic BP was kept above 140 mmHg during cross-clamping.

For the TCD registration, a pulsed Doppler transducer (Pioneer TC4040, EME, Überlingen, Germany), gated at a focal depth of 45–60 mm, was placed over the temporal bone to insonate the main stem of the ipsilateral MCA, with the TCD transducer being fixed with a head frame and V_{mean} was recorded continuously. The values used for further analysis were gathered in real time on indicated data points as described below.

Post-CEA anti-hypertensive treatment protocol

All patients with PH, that is, BP >160 mmHg systolic (absolute), >20% above the preoperative BP, or BP risen above the individual restriction in patients with an intra-operative V_{mean} increase >100%, underwent strict individualised BP control during the early post-operative period. Anti-hypertensive treatment consisted of intravenous labetalol (first choice) or clonidine (second choice). If BP was not controlled appropriately after 6 h on the recovery ward, the patient was transferred to the medium care unit (MCU) for continuous BP monitoring and treatment until BP reached the appropriate limits. If BP was within the required limits, intravenous anti-hypertensive treatment was tapered as soon as possible and an oral beta-blocker (labetalol or metoprolol) was started. If PH occurred on the nursing ward, oral beta-blockers (labetalol or metoprolol) were given firstly. However, if the BP was not sufficiently controlled or even increased, whether or not in combination with neurological symptomatology, (re)transfer to the MCU was established.

Timeframes

Four timeframes were indicated, which are schematically shown in Fig. 1.

For the preoperative V_{mean} (V_1), a TCD measurement of the MCA ipsilateral to the treated carotid artery was performed within 1 week prior to operation. During operation, the pre-clamping V_{mean} (V_2) was registered 30 s prior to carotid cross-clamping. The post-declamping V_{mean} (V_3) was determined 3 min after declamping. An additional postoperative V_{mean} (V_4) was measured within the first hour after arrival on the recovery ward. All patients received their

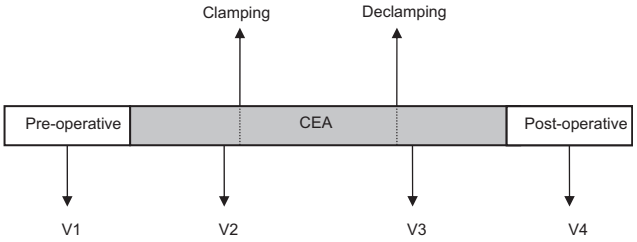

Figure 1. Timeline TCD measurements around CEA. V_1: Preoperative mean blood velocity (V_{mean}) prior to CEA. V_2: Pre-clamping V_{mean} measured at most 1 min before carotid clamping. V_3: Post-declamping V_{mean} measured 3 min after carotid declamping. V_4: Postoperative V_{mean} measured within the first 2 h on the recovery warm.

last TCD measurement within the first 2 h after surgery. This V_4 measurement was performed in all patients in the UMCU, but mainly in case of hypertension or an increased V_3 in the St. Antonius hospital.

The *intra-operative* increase of V_{mean} was defined and calculated as follows:

$$(V_3 - V_2)/V_2 \times 100\%.$$

For calculating the 'postoperative' increase of V_{mean} the following formula was used:

$$(V_4 - V_1)/V_1 \times 100\%.$$

Statistical analysis

Patients were classified according to the relative increase in V_{mean} (i.e., less or more than 100% increase) at predefined two timeframes (intra-operatively and postoperatively) in relation to CHS occurrence (Fig. 1).

The positive predictive value (PPV) and negative predictive value (NPV) of both intra-operative and postoperative increase of V_{mean} were calculated. Differences in BP between the intra-operative and postoperative measurements and between CHS and non-CHS groups were compared using the Chi-square test for categorical variables and Student's *t*-test or Mann–Whitney *U* test for continuous variables, as appropriate. These statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) 15.0 software. A confidence level of less than 5% ($p < 0.05$) was considered significant.

Results

Patient characteristics

In the St. Antonius Hospital Nieuwegein 560 patients underwent CEA during the time of the study. Of these 560, 72 (13%) received both intra- and postoperative TCD monitoring and were included for the present analysis. In the UMCU, a postoperative TCD measurement was performed in 112 of 211 patients (53%) who underwent CEA within the time frame February 2009–August 2010. Therefore, out of 771 patients a total of 184 patients were included in this study (Table 1). In both hospitals, patients were excluded for the study because of logistic reasons.

The majority of patients were symptomatic (159 patients, 87%). Thirty-three patients (18%) required the use of an intra-luminal shunt because of either EEG asymmetry or a decrease of >60% of V_{mean} measured by TCD. After stratification according to hospital, the majority of patients' characteristic parameters were comparable. Three variables significantly differed between the St. Antonius and the UMCU: alcohol usage (54% vs. 76%, $p = 0.005$, respectively), PH (26% vs. 13%, $p = 0.027$, respectively) and shunt use (31% vs. 10%, $p < 0.001$, respectively).

TCD measurements

Sixteen patients (9%) had an intra-operative V_{mean} increase >100% (Fig. 2; B). Postoperatively, a V_{mean} increase >100% was found in an additional 15 patients (8%) (Fig. 2; D and F). In seven patients (4%) both the intra-operative and the postoperative measurement showed a V_{mean} increase >100% (Fig. 2; D).

During all TCD measurements the systolic BP was significantly lower after declamping compared to the pre-clamping systolic BP,

Table 1
Patient characteristics.

Patient characteristics	Combined $N = 112$	UMCU $N = 112$	St. Antonius Hospital $N = 72$	*P*-value
	Mean (±SD)	*Mean (±SD)*	*Mean (±SD)*	
Age (yrs)	68.8 (±9.9)	69.1 (±9.8)	68.4 (±10.1)	0.68
	Number of patients (%)			
Gender (male)	141 (77%)	88 (79%)	53 (74%)	0.438
Risk factors				
Diabetes	36 (20%)	26 (23%)	10 (17%)	0.330
Hypertension	135 (73%)	85 (76%)	50 (69%)	0.334
Hypercholesterolaemia	164 (89%)	102 (91%)	62 (86%)	0.436
Coronary artery disease	50 (27%)	36 (32%)	14 (20%)	0.091
Smoking	61 (33%)	43 (38%)	18 (25%)	0.077
Alcohol use	124 (67%)	85 (76%)	39 (54%)	0.005
Site (right)	83 (45%)	47 (42%)	36 (50%)	0.285
Symptomatic	159 (87%)	97 (87%)	62 (86%)	0.924
Degree of stenosis (ipsilateral)				
>70%	174 (95%)	106 (95%)	68 (94%)	0.901
≥ 50%	10 (5%)	6 (5%)	4 (5%)	
Degree of contralateral stenosis				
Occlusion	27 (15%)	15 (13%)	12 (17%)	
Stenosis >70%	17 (9%)	12 (11%)	5 (7%)	0.257
Stenosis 50–70%	30 (16%)	18 (16%)	12 (17%)	
Stenosis <50%	94 (51%)	61 (55%)	33 (46%)	
Unknown	16 (9%)	10 (%)	6 (14%)	
Shunt use	33 (18%)	11 (10%)	22 (31%)	<0.001
Post-operative hypertension	34 (19%)	15 (13%)	19 (26%)	0.027
Cerebral hyperperfusion syndrome	10 (5%)	5 (5%)	5 (7%)	0.469

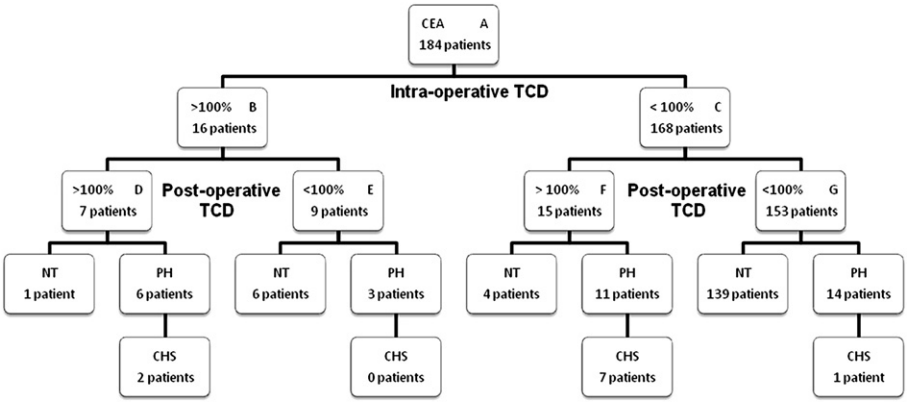

Figure 2. Flowchart. Intra-operative TCD: TCD increase 3 min after declamping as compared to the pre-clamping values. Postoperative TCD: TCD increase on the recovery room in the first 2 h postoperatively compared to the preoperative values. NT: Normotensive. PH: Postoperative hypertension. CHS: Cerebral hyperperfusion syndrome.

the mean decrease was 11.3 mmHg (95% confidence interval (C.I.) 7.3–15). Postoperatively, the systolic BP was 4.0 mmHg lower (95% C.I. −12.6 to −20.6) compared to the preoperative systolic BP.

Clinical outcome

Of all 184 patients, one (0.5%) patient had an intra-operative stroke. Postoperatively, 34 patients (19%) developed PH and 10 patients (5%) suffered from CHS. All 10 patients with CHS had hypertension during the postoperative phase. Nine fully recovered, but one patient refused further treatment and died because of intracranial haemorrhage. The overall 30-day rate of death/stroke was 1%.

TCD measurements and clinical outcome

Of 16 patients with an intra-operative increase of V_{mean} >100% (Fig. 2; B), nine developed PH and, of these, two patients developed CHS. On the other hand, in 168 patients who had an intra-operative increase less than 100% (Fig. 2; C), 25 patients developed PH and eight of them suffered from CHS. This results in a PPV of 56% (9/16) and a NPV of 85% (143/166) in the prediction of PH and a PPV of 13% (2/16) and NPV of 95% (160/168) in the prediction of CHS (Tables 2 and 3).

With respect to the postoperative TCD measurements 17 of the 22 patients with a doubling of postoperative V_{mean} (Fig. 2; D and F) developed PH and in nine of them CHS occurred. In the subgroup of 162 patients with postoperative increase of less than 100% (Fig. 2; E and G), 17 patients developed PH and one patient CHS. This results in a PPV of 77% (17/22) and a NPV of 90% (145/162) for PH and a PPV 41% (9/22) and a NPV of 99% (161/162) for the development of CHS (Tables 2 and 3).

Of all 31 patients, who had an intra-operative and/or post-operative V_{mean} increase of more than 100% (Fig. 2; B and F), 20 developed PH and nine CHS. Only one patient with CHS did not have postoperative V_{mean} doubling. Of the 153 patients without an increase >100% at any time point (Fig. 2; G), 14 patients developed PH and one patient developed CHS. This results in a PPV of 65% (20/31) and NPV of 91% (139/153) for the prediction of postoperative hypertension and a PPV of 29% (9/31) and NPV of 99% (152/153) for the development of CHS.

CHS versus non-CHS

The median (interquartile range) intra-operative V_{mean} increase was 10% (0–31) in the non-CHS group ($n = 174$) and 23% (5–85) in CHS patients ($n = 10$; $p = 0.122$). The differences in median post-operative V_{mean} increase was 18% (1–47) in the non-CHS and 107% (99–115) in the CHS group respectively ($p < 0.005$) (Fig. 3).

PH occurred in all 10 patients who developed CHS (100%) and in only 24 patients out of 174 (14%) in the non-CHS group ($p < 0.005$).

There was no significant difference in intra-operative BP changes between the CHS and non-CHS group neither during the intra-operative measurements ($p = 0.234$) nor during the post-operative measurements ($p = 0.463$).

Discussion

An increase in V_{mean} measured postoperatively predicts the development of CHS better than the commonly used increase in V_{mean} measured 3 min after declamping versus pre-clamping value. The PPV of the postoperative measurement in the prediction of CHS is more than three times higher than of the intra-operative measurement (41% and 13%, respectively). Thus, for 28% of the patients who developed CHS in our cohort, this complication would have been predicted in an early stage if a postoperative TCD measurement had been performed. Moreover, the absence of doubling of the V_{mean} at the postoperative measurement excluded the development of CHS almost completely. Therefore, with post-operative measurement fewer patients will be treated unnecessarily by strict intravenous anti-hypertensive medication.

The association between changes in cerebral artery flow after CEA and the development of CHS has been extensively described.[23] In 1988 Piepgras et al. showed that doubling of the CBF measured by intra-carotid injection of xenon-133, was associated with the occurrence of intra-cerebral haemorrhage.[14] Nowadays, TCD, which is relatively inexpensive and does not require radiation exposure is widely applied for monitoring in CEA.

A critical issue is to what extent blood velocity reflects on actual volume flow. In the unlikely case that blood flow is not laminar, the blood velocity changes out of proportion with volume flow. Second, changes in velocity are parallel with volume flow only when both the angle of insonation and the diameter of the vessel remain constant. The large cerebral arteries are conductance rather than resistance vessels and changes in systemic arterial blood pressure within the physiological range appear to have a negligible effect on the diameter of the insonated artery.[24,25] Third, validation studies found that changes in mean middle cerebral artery blood velocity follow cerebral 133Xe clearance.[26,27] Technical limitations of TCD include the lack of sufficient bone window in 10–15% of patients. Furthermore, TCD monitoring, like many other diagnostic techniques, is operator-dependent and requires training and experience

Table 2
Predictive values of TCD measurements for the occurrence of CHS at different timeframes (capitals refer to Fig. 2).

		CHS+	CHS−	PPV (%)	NPV (%)
Combined data					
Intra-operative increase					
>100% (B)		2 (1%)	14 (8%)	13	95
<100% (C)		8 (5%)	160 (86%)		
Post-operative increase					
>100% (D + F)		9 (5%)	13 (7%)	41	99
<100% (E + G)		1 (1%)	161 (87%)		
Intra-operative increase	Post-operative increase				
>100%	>100% (D)	2 (1%)	5 (3%)	29	95
>100%	<100% (E)	0 (0%)	9 (5%)	0	94
<100%	>100% (F)	7 (4%)	8 (4%)	47	98
<100%	<100% (G)	1 (1%)	152 (82%)	1	71
Total (%)		10 (6%)	174 (94%)		
St. Antonius Hospital (retrospectively included data)					
Intra-operative increase					
>100% (B)		2 (3%)	10 (14%)	17	95
<100% (C)		3 (4%)	57 (79%)		
Post-operative increase					
>100% (D + F)		5 (7%)	8 (11%)	38	100
<100% (E + G)		0	59 (82%)		
Intra-operative increase	Post-operative increase				
>100%	>100% (D)	2 (3%)	4 (6%)	33	95
>100%	<100% (E)	0	6 (8%)	0	92
<100%	>100% (F)	3 (4%)	4 (6%)	43	97
<100%	<100% (G)	0	53 (73%)	0	74
Total (%)		5 (7%)	67 (93%)		
UMCU (prospectively included data)					
Intra-operative increase					
>100% (B)		0	4 (4%)	0	95
<100% (C)		5 (4%)	103 (92%)		
Post-operative increase					
>100% (D + F)		4 (4%)	5 (4%)	44	99
<100% (E + G)		1 (1%)	102 (91%)		
Intra-operative increase	Post-operative increase				
>100%	>100% (D)	0	1 (1%)	0	95
>100%	<100% (E)	0	3 (2%)	0	95
<100%	>100% (F)	4 (4%)	4 (4%)	50	99
<100%	<100% (G)	1 (1%)	99 (88%)	1	67
Total (%)		5 (4%)	107 (96%)		

CHS+: number of patients who developed CHS (%). CHS−: number of patients who did not develop CHS (%). PPV: positive predictive value (%). NPV: negative predictive value (%).

Table 3
Predictive values of TCD measurements for the occurrence of post-operative hypertension (PH) at different timeframes (capitals refer to Fig. 2).

		PH+	PH−	PPV (%)	NPV (%)
Intra-operative increase					
>100% (B)		9 (5%)	7 (4%)	56	85
<100% (C)		25 (13%)	143 (78%)		
Post-operative increase					
>100% (D + F)		17 (9%)	5 (3%)	77	90
<100% (E + G)		17 (9%)	145 (79%)		
Intra-operative increase	Post-operative increase				
>100%	>100% (D)	6 (3%)	1 (1%)	86	84
>100%	<100% (E)	3 (2%)	6 (3%)	33	82
<100%	>100% (F)	11 (6%)	4 (2%)	73	86
<100%	<100% (G)	14 (7%)	139 (76%)	9	35
Total (%)		34 (18%)	150 (82%)		

PH+: number of patients who developed PH (%). PH−: number of patients who did not develop PH (%). PPV: positive predictive value (%). NPV: negative predictive value (%).

to perform and interpret results correctly. Nevertheless, as the measurements were performed by experienced personnel, the reproducibility of TCD measurement is high. According to literature, TCD determination of V_{mean} are reproducible with a difference of less than 3% with $R = 0.95$.

Ogasawara et al. showed that the accuracy of intra-operative TCD monitoring is less reliable in predicting CHS than TCD at the end of the procedure.[20] However, they defined postoperative TCD as 'at the end of the procedure at the operating room', while the patient was still influenced by anaesthetic medication. As anaesthetics may reduce cerebral blood flow, these values could not be reliably compared with preoperative TCD values. As far as we know, analysis or studies comparing the accuracy of postoperatively with intra-operatively measured TCD values in the prediction of CHS have never been performed. Therefore, besides determination of the cerebrovascular reserve capacity with 123I-IMP SPECT[13] or TCD[28] after acetazolamide administration, preoperative selection of patients at risk to develop CHS is not yet possible, since well-known patient factors supposedly predisposing for CHS have not been clarified, or have been analysed for a single risk factor only.[8]

In our study, only 10 of patients developed CHS. The low incidence of CHS hampers the interpretation of our results. This small number did not allow multivariate statistical analysis (logistic regression). However, the incidence in our group (5%) of patients is relatively high compared to other series. This might be explained by the fact that in our referral hospitals a selected group of patients with relatively severe haemodynamic compromise are treated. To determine the influence of the retrospective inclusion of the St. Antonius Hospital patient cohort, analyses on outcome were stratified according to hospital. The first variable that significantly differed between both hospitals was alcohol use, which we believe is coincidence and does not affect the risk for CHS. Furthermore, postoperative hypertension and the use of an intra-operative shunt was more frequently present in the St. Antonius patients. This can be explained by the fact that postoperative TCD was preferentially performed in patients with PH or an intra-operative V_{mean} increase of >100%. Also the use of intra-operative shunting was believed to potentially increase the risk of CHS and, as a consequence, this was

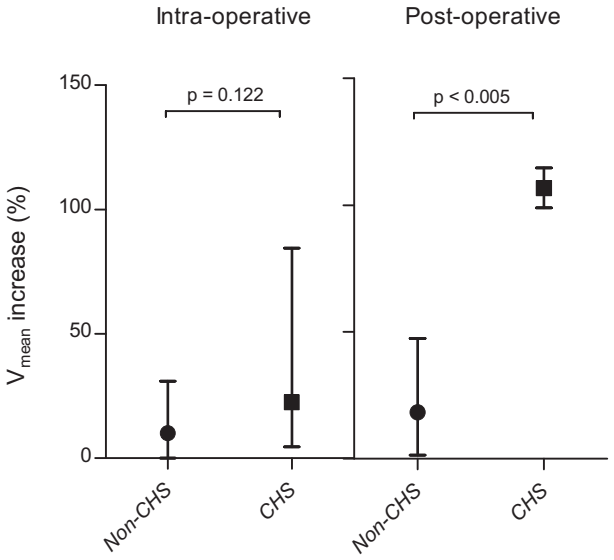

Figure 3. V_{mean} increase for CHS and non-CHS patients. Intra- and postoperative V_{mean} increase in patients who developed CHS ($n = 10$) and patients who did not ($n = 174$). Values are median with interquartile range.

reflected by the difference in shunt use between the St. Antonius and UMCU (31% vs. 10%, $p < 0.001$, respectively, Table 1).

As patients were followed up by a postoperative TCD measurement, but being treated (for BP control) based on the intra-operative TCD measurement, this approach might have led to an underestimation of the predictive value of intra-operative measurements in the UMCU.

Nevertheless, the difference in incidence of CHS between the prospectively and retrospectively included data was small and non-significant (5% vs. 7%, respectively; Table 1) and the predictive values were almost identical in both hospitals. Importantly, in both hospitals the majority of CHS patients being identified by post-operative TCD but being missed by intra-operative TCD were significant in both hospitals (Table 2). Thus, the assumption that postoperative measurement improves identification of patients at risk for CHS was confirmed in each hospital separately in equal measures. These findings further underline the lack of significant preoperative and intra-operative prediction models for CHS development by technical aspects of the procedure.

We assume that the changes in V_{mean} could not be explained by the differences in BP among the several TCD measurements, since the changes in BP were inversely correlated to the changes in V_{mean} (increase) for the intra-operative measurements and no significant change in MAP was found between the pre- and postoperative TCD measurements.

In conclusion, besides the commonly used intra-operative TCD monitoring, additional TCD measurement in the early post-operative phase is useful to predict CHS in patients who underwent CEA under general anaesthesia. However, this observation needs to be validated for patients undergoing CEA under local anaesthesia. Furthermore, most patients who develop CHS do so following prior PH development. Therefore, anti-hypertensive treatment for all patients having PH should be administered appropriately since they are at risk to develop CHS subsequently.

By measuring V_{mean} in the postoperative instead of only in the intra-operative phase, both the positive and negative predictive values of TCD for development of CHS after CEA can be improved. Therefore, we recommend a baseline measurement before the administration of anaesthetics and a postoperative measurement within 2 h after surgery.

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No other persons have made substantial contributions to this manuscript.

Ethical Approval for Research

Ethics committee approval was not necessary as all performed procedures were part of routine clinical protocol.

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Conflict of Interest

W.F. Buhre receives honoraria from Edwards Life sciences hemodynamic monitoring.

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